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DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 233

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AB This invention relates to compds. and methods useful for modulating EGFR gene (e.g., HER1, HER2, HER3, and/or HER4) expression by RNAi using siNA's. The siNA's may include siRNA and modified siRNA, double-stranded RNA, micro-RNA, and short hairpin RNA mols.. The siNA's may be used in the treatment of cancer. Thus, chemical modified siRNA's significantly reduced HER1 and HER2 gene expression in vitro in A549 (ovarian cancer) cells.

ANSWER 2 OF 14 CA COPYRIGHT 2006 ACS on STN L5

ACCESSION NUMBER:

142:386024 CA

TITLE:

Nucleic acid treatment of diseases or conditions

related to expression levels of RAS, HER2

and HIV genes

INVENTOR(S):

McSwiggen, James

PATENT ASSIGNEE(S):

Sirna Therapeutics, Inc., USA

SOURCE:

U.S. Pat. Appl. Publ., 143 pp., Cont.-in-part of U.S.

Ser. No. 693,059.

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AB The present invention relates to nucleic acid mols., including enzymic nucleic acid mols., that modulate the expression of Ras genes (such as K-RAS, H-RAS, and/or N-RAS), HER2 gene, and HIV genes. Gene sequences of human c-Ki-ras2, c-Ha-ras1, and HER2 genes and HIV-1 genes were screened for accessible sites using a computer-folding algorithm. DNAzymes are designed for c-Ki-ras2, c-Ha-ras1, and HER2; for modulation of HIV-1 genes, the present invention provides DNAzymes, hammerhead ribozymes, Inozymes, Zinzymes, Amberzymes, and other enzymic nucleic acids.

L5 ANSWER 3 OF 14 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 142:183225 CA

TITLE: RNA interference-mediated inhibition of gene

expression using chemically modified short interfering

nucleic acids

INVENTOR(S): McSwiggen, James; Chowrira, Bharat; Beigelman, Leonid;

Macejak, Dennis; Zinnen, Shawn; Pavco, Pamela; Haeberli, Peter; Morissey, David; Fosnaugh, Kathy; Jamison, Sharon; Usman, Nassim; Thompson, James;

Vargeese, Chandra; Wang, Weimen; Chen, Tonqian; Vaish,

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PATENT ASSIGNEE(S):

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AB The present invention concerns methods and reagents useful in modulating gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to synthetic chemical modified small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against target nucleic acid sequences. Introduction of chemical modified nucleotides into nucleic acid mols. provides a powerful tool in overcoming potential limitations of in vivo stability and bioavailability inherent to native RNA mols. Unlike native unmodified siRNA, chemical modified siNA can also minimize the possibility of activating interferon activity in humans. Modifications are described including pyrimidine or purine nucleotides with 2'-deoxy-2'-fluoro or 2'-O-Me groups, phosphorothioate backbone modification, terminal residues comprising inverted deoxy thymidine or inverted deoxy abasic moieties, linking the sense and antisense strands with glyceryl succinate or dodecanoic acid or other linkers, and conjugation of targeting ligands (N-acetylgalactosamine, pteroic acid, peptides, or phospholipids) to the oligonucleotide termini. Thus, the serum stability of siNA constructs consisting of all RNA nucleotides containing two thymidine nucleotide overhangs have a half-life in human serum of 15 s, whereas chemical modified siNA constructs remained stable in serum for 1 to 3 days depending on the extent of modification. The small nucleic acid mols. are useful in the treatment of any disease or condition that responds to modulation of gene expression or activity in a cell, tissue, or organism. Three nuclease-resistant siNA mols. targeting site 1580 of hepatitis B virus RNA are designed using Stab 7/8 chemical and a 5'-terminal conjugate moiety (a branched cholesterol conjugate, a branched phospholipid conjugate, and a polyethylene glycol conjugate) showed significant stability in human and mouse serum (t1/2 = 10-408 h) and human liver extract (t1/2 = 28-43 h); the most stable siNA with all purine positions in the antisense strand with 2'-O-Me nucleotides had a half-life of 816 h in human liver extract

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RNA interference-mediated inhibition of gene expression using chemically modified short interfering nucleic acids

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The present invention concerns methods and reagents useful in modulating gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to synthetic chemical modified small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against target nucleic acid sequences. Introduction of chemical modified nucleotides into nucleic acid mols. provides a powerful tool in overcoming potential limitations of in vivo stability and bioavailability inherent to native RNA mols. Unlike native unmodified siRNA, chemical modified siNA can also minimize the possibility of activating interferon activity in humans. Modifications are described including pyrimidine or purine nucleotides with 2'-deoxy-2'-fluoro or 2'-O-Me groups, phosphorothioate backbone modification, terminal residues comprising inverted deoxy thymidine or inverted deoxy abasic moieties, linking the sense and antisense strands with glyceryl succinate or dodecanoic acid or other linkers, and conjugation of targeting ligands (N-acetylgalactosamine, pteroic acid, peptides, or phospholipids) to the oligonucleotide termini. Thus, the serum stability of siNA constructs consisting of all RNA nucleotides containing two thymidine nucleotide overhangs have a half-life in human serum of 15 s, whereas chemical modified siNA constructs remained stable in serum for 1 to 3 days depending on the extent of modification. The small nucleic acid mols. are useful in the treatment of any disease or

AB

condition that responds to modulation of gene expression or activity in a cell, tissue, or organism. Three nuclease-resistant siNA mols. targeting site 1580 of hepatitis B virus RNA are designed using Stab 7/8 chemical and a 5'-terminal conjugate moiety (a branched cholesterol conjugate, a branched phospholipid conjugate, and a polyethylene glycol conjugate) showed significant stability in human and mouse serum (t1/2 = 10-408 h) and human liver extract (t1/2 = 28-43 h); the most stable siNA with all purine positions in the antisense strand with 2'-O-Me nucleotides had a half-life of 816 h in human liver extract

ANSWER 5 OF 14 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 139:240342 CA

TITLE: RNA interference mediated inhibition of gene

expression using chemically modified short interfering

INVENTOR(S): Mcswiggen, James; Beigelman, Leonid; Chowrira, Bharat;

Pavco, Pamela; Fosnaugh, Kathy; Jamison, Sharon;

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PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 593 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 233

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The present invention concerns methods and reagents useful in modulating AB gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against target nucleic acid sequences. Exemplary siNA mols. are synthesized in tandem using standard phosphoramidite synthesis chemical and a cleavable linker, for example a succinyl-based linker, followed by a one-step purification process that provides RNAi mols. in high yield. Chemical modifications (2'-O-Me and 2'-deoxy-2'-fluoro groups, phosphorothioate linkages, 5'-terminal caps comprising an inverted deoxy abasic moiety, etc.) in siNA constructs are selected to yield nuclease resistance while preserving the ability to mediate RNAi activity. The siNA mols. are designed that can bind to target mRNAs for vascular endothelial growth factor receptors, BCL2, HER2/ neu/c-Myc, PCNA, RELA, PTP1B, BACE, CHK1, PKC- α , and EGFR/HER1, and are optionally individually analyzed by a computer folding algorithm to assess whether the siNA mol. can interact with the target sequence. The siNA mols. are useful in the treatment and diagnosis of any condition that responds to modulation of gene expression or activity in a cell, tissue, or organism.

L5 ANSWER 6 OF 14 CA COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:191417 CA
TITLE: RNA interference-mediated inhibition of epidermal

growth factor receptor gene expression using short interfering nucleic acids
McSwiggen, James: Pavco, Pamela; Beigelman, Leonid

INVENTOR(S): McSwiggen, James; Pavco, Pamela; Beigelman, Leonid; Fosnaugh, Kathy; Jamison, Sharon

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Incorporated, USA; Sirna

Therapeutics, Inc.

SOURCE: PCT Int. Appl., 171 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 233

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AB The present invention concerns methods and reagents useful in modulating epidermal growth factor receptor gene (HER1, HER2 also known as erbB2/neu, HER3, and HER4) expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against epidermal growth factor receptor gene expression and/or activity. Exemplary siNA mols. are synthesized in tandem using standard phosphoramidite synthesis chemical

and a cleavable linker, for example a succinyl-based linker, followed by a one-step purification process that provides RNAi mols. in high yield. Chemical modifications (2'-O-Me and 2'-deoxy-2'-fluoro groups, phosphorothioate linkages, 5'-terminal caps comprising an inverted deoxy abasic moiety, etc.) in siNA constructs are selected to yield nuclease resistance while preserving the ability to mediate RNAi activity. The siNA mols. are designed that can bind to each target and are optionally individually analyzed by a computer folding algorithm to assess whether the siNA mol. can interact with the target sequence. The efficacy of siNAs targeting epidermal growth factor receptor genes are tested in cell culture using, for example, SKBR-3 or SKOV-3 cells, to detn the extent of RNA and protein inhibition; after an optimal transfection agent concentration is chosen, a RNA time-course of inhibition is performed

the lead siNA mol(s). The siNA mols. are useful in the treatment and diagnosis of cancer.

ANSWER 7 OF 14 CA COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 139:240335 CA TITLE:

RNA interference-mediated inhibition of epidermal growth factor receptor gene expression using short

interfering nucleic acids

INVENTOR (S): McSwiggen, James A. USA

PATENT ASSIGNEE(S):

with

U.S. Pat. Appl. Publ., 307 pp., Cont.-in-part of U.S. Ser. No. 163,552. SOURCE:

CODEN: USXXCO

DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: 233

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OTHER SOURCE(S): MARPAT 139:240335

The present invention concerns methods and reagents useful in modulating epidermal growth factor receptor gene (HER1, HER2 also known as erbB2/neu, HER3, and HER4) expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against epidermal growth factor receptor gene expression and/or activity. Exemplary siNA mols. are synthesized in tandem using standard phosphoramidite synthesis chemical

and a cleavable linker, for example a succinyl-based linker, followed by a one-step purification process that provides RNAi mols. in high yield. Chemical modifications (2'-O-Me and 2'-deoxy-2'-fluoro groups, phosphorothioate linkages, 5'-terminal caps comprising an inverted deoxy abasic moiety, etc.) in siNA constructs are selected to yield nuclease resistance while preserving the ability to mediate RNAi The siNA mols. are designed that can bind to each target and activity. are optionally individually analyzed by a computer folding algorithm to assess whether the siNA mol. can interact with the target sequence. The efficacy of siNAs targeting epidermal growth factor receptor genes are tested in cell culture using, for example, SKBR-3 or SKOV-3 cells, to detn the extent of RNA and protein inhibition; after an optimal transfection agent concentration is chosen, a RNA time-course of inhibition is performed

the lead siNA mol(s). The siNA mols. are useful in the treatment and diagnosis of cancer.

ANSWER 8 OF 14 CA COPYRIGHT 2006 ACS on STN DUPLICATE 1 ACCESSION NUMBER:

138:19530 CA

TITLE: Nucleic acid treatment of diseases or conditions

related to levels of Ras, HER2 and HIV

INVENTOR (S): McSwiggen, James

PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Incorporated, USA

SOURCE: PCT Int. Appl., 185 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 233

PATENT INFORMATION:

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The present invention relates to nucleic acid mols., including enzymic nucleic acid mols., such as DNAzymes (e.g. DNA enzymes, catalytic DNA), siRNA, aptamers, and antisense that modulate the expression of Ras genes such as K-Ras, H-Ras, and/or N-Ras, HIV genes such as HIV-1, and HER2 (c-erbB2) gene. The sequence of human HER2 or Ras genes were screened for accessible sites using a computer-folding algorithm. Regions of the RNA that do not form secondary folding structure and contain potential enzymic nucleic acid mol. and/or antisense binding/cleavage sites are identified. The sequences of c-Ki-ras, c-Ha-ras, HER2, and HIV RNA binding/cleavage sites are provided, as are the sequences of designed enzymic nucleic acid mols., e.g., hammerhead ribozymes, DNAzymes, inozymes, zinzymes, and Amberzymes. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L5 ANSWER 9 OF 14 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 137:104780 CA

TOTAL

TITLE: Method for inhibiting the expression of a target gene

INVENTOR(S): Kreutzer, Roland; Limmer, Stephan; Rost, Sylvia;

Hadwiger, Philipp

PATENT ASSIGNEE(S): Ribopharma Ag, Germany SOURCE: PCT Int. Appl., 203 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 13

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WO 2002-EP11973 W 20021025

AB A method of inhibiting the expression of a specific gene using double-stranded oligoribonucleotides (dsRNA) capable of hybridizing with the gene is described. The dsRNA has a double-stranded core that is no more than 49 base-pairs long and has one or two 1-4 nucleotide single-stranded ends. Inhibition of expression of green fluorescent protein reporter gene in vitro and in vivo (3T3 and HeLa-S3 cells) by double-stranded RNA was demonstrated. A 21-nucleotide oligoribonucleotide, to which the complementary oligoribonucleotide was covalently attached via a linker, was shown to be an effective inhibitor. Inhibition of expression of the genes for epidermal growth factor receptors in the glioblastoma cell line U87MG is demonstrated.

L5 ANSWER 10 OF 14 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 137:104740 CA

TITLE: Targeted inhibition of gene expression with

double-stranded RNA with single-stranded ends INVENTOR(S): Kreutzer, Roland; Limmer, Stefan; Rost, Sylvia;

Hadwiger, Philipp

PATENT ASSIGNEE(S): Ribopharma A.-G., Germany

SOURCE: Ger. Offen., 100 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

DE 10100588 A1 20020718 DE 2001-10100588 20010109 <-PRIORITY APPLN. INFO.: DE 2001-10100588 20010109

20010109 A method of inhibiting the expression of a specific gene using double-stranded oligoribonucleotides (dsRNA) capable of hybridizing with the gene is described. The dsRNA has a double-stranded core that is no more than 49 base-pairs long and has 1-4 nucleotide single-stranded ends. The RNA may be delivered as single-stranded RNAs that hybridize to create the duplex, e.g. as nucleotide-resistant phosphorothioate oligonucleotides. The RNA may be made up of three oligonucleotides with the overlaps between the individual pairs of oligonucleotides being no more than 25 base pairs. This structure ensures that the ends are in the same orientation with respect to the target sequence. Inhibition of expression of green fluorescent protein reporter gene in vitro and in vivo (3T3 cells) by double-stranded RNA was demonstrated. A 21-nucleotide oligoribonucleotide, to which the complementary oligoribonucleotide was covalently attached via a linker, was shown to be an effective inhibitor.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 14 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 137:380906 CA

TITLE: Inhibition of gene expression with double-stranded

oligoribonucleotides in interferon-treated cells Kreutzer, Roland; Limmer, Stefan; Rost, Sylvia;

Hadwiger, Philipp

PATENT ASSIGNEE(S): Ribopharma AG, Germany

SOURCE: Ger., 98 pp.
CODEN: GWXXAW

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

INVENTOR (S):

PATENT NO. KIND DATE APPLICATION NO. DATE

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PRIORITY APPLN. INFO.:
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     The invention concerns a method for inhibiting expression of a target gene
     in a cell comprising introducing at least one double-stranded
     oligoribonucleotide (dsRNA) of no more than 49 bp in a
     sufficient quantity for the inhibition of the expression of the target
            Preferably, at least one end of the dsRNA contains
     gene.
     non-Watson-Crick-paired nucleotides, or consists of 1-4 unpaired
     nucleotides. One strand, or a portion of one strand, of the dsRNA
     is complementary to the target gene. The cell is treated with interferon
     before induction of the dsRNA.
REFERENCE COUNT:
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                     CA COPYRIGHT 2006 ACS on STN
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     ANSWER 12 OF 14
ACCESSION NUMBER:
                         136:305087 CA
TITLE:
                         Targeted inhibition of gene expression with
                         double-stranded RNA with single-stranded ends
INVENTOR(S):
                         Kreutzer, Roland; Limmer, Stefan; Rost, Sylvia;
                         Hadwiger, Philipp
PATENT ASSIGNEE(S):
                         Ribopharma A.-G., Germany
SOURCE:
                         Ger., 104 pp.
                         CODEN: GWXXAW
DOCUMENT TYPE:
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LANGUAGE:
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FAMILY ACC. NUM. COUNT:
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EP 1352061

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PRIORITY APPLN. INFO.:
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     A method of inhibiting the expression of a specific gene using
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     double-stranded oligoribonucleotides (dsRNA) capable of
     hybridizing with the gene is described. The dsRNA has a
     double-stranded core that is no more than 49 base-pairs long and has 1-4
     nucleotide single-stranded ends. Inhibition of expression of green
     fluorescent protein reporter gene in vitro and in vivo (3T3 cells) by
     double-stranded RNA was demonstrated. A 21-nucleotide
     oligoribonucleotide, to which the complementary oligoribonucleotide was
     covalently attached via a linker, was shown to be an effective inhibitor.
REFERENCE COUNT:
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     ANSWER 13 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:
                   2003064850 EMBASE
                   The effectiveness of double-stranded short inhibitory RNAs
TITLE:
                   (siRNAs) may depend on the method of
                   transfection.
AUTHOR:
                   Walters D.K.; Jelinek D.F.
CORPORATE SOURCE:
                   Dr. D.F. Jelinek, 200 First Street, S. W., Rochester, MN
                   55905, United States. jelinek.diane@mayo.edu
                   Antisense and Nucleic Acid Drug Development, (2002) Vol.
SOURCE:
                   12, No. 6, pp. 411-418. .
                   Refs: 17
                   ISSN: 1087-2906 CODEN: ANADF5
COUNTRY:
                   United States
DOCUMENT TYPE:
                   Journal; Article
FILE SEGMENT:
                   016
                           Cancer
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                           Human Genetics
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LANGUAGE:
                   English
SUMMARY LANGUAGE:
                   English
ENTRY DATE:
                   Entered STN: 20 Feb 2003
                   Last Updated on STN: 20 Feb 2003
    RNA interference (RNAi) is a recently described powerful
AB
     experimental tool that can cause sequence-specific gene silencing, thereby
     facilitating functional analysis of gene function. Consequently, we
    became interested in using RNAi to determine the function of
    aberrantly expressed ErbB3 in the KAS-6/1 human myeloma cell line.
    Despite the wealth of information available on the use of RNAi,
    dsRNA target design, and the transfection of dsRNA in
    vitro, little information is available for transfecting dsRNA
    into nonadherent cells from any species. In the present study, we report
    that gene silencing of ErbB3 was not observed in myeloma cells when
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dsRNA targeting ErbB3 was introduced using conventional

transfection agents and protocols that have proved successful for several adherent cell lines. Silencing of ErbB3, however, was observed in T47D cells, an adherent breast carcinoma cell line, using the same transfection methods, indicating that our target sequence was functional for gene silencing of ErbB3. Interestingly, ErbB3 was silenced in myeloma cells when the dsRNA target was introduced by electroporation. Thus, our studies illustrate the striking dependence of dsRNA-mediated gene silencing in some cells on the methods of dsRNA transfection.

L5 ANSWER 14 OF 14 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 91347216 MEDLINE DOCUMENT NUMBER: PubMed ID: 1715233

TITLE: A distinct kinase modulates the expression of IFN-inducible

genes in human breast cancer cells.

AUTHOR: Tiwari R K; Osborne M P

CORPORATE SOURCE: Breast Cancer Research Laboratory, Memorial Sloan Kettering

Cancer Center, New York, N.Y. 10021.

CONTRACT NUMBER: P-01 CA29502 (NCI)

SOURCE: Cancer letters, (1991 Jul 26) Vol. 59, No. 1, pp.

31-6.

Journal code: 7600053. ISSN: 0304-3835.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199110

ENTRY DATE: Entered STN: 20 Oct 1991

Last Updated on STN: 3 Mar 2000 Entered Medline: 2 Oct 1991

AB The biological activity of interferons (IFNs) is presumed to be mediated through the induction of a number of IFN-inducible genes. IFN-mediated gene induction was examined in two human breast cancer cell lines, MCF-7 and BT-20. Both these cell lines were remarkably responsive to IFNs as a number of IFN inducible genes were rapidly induced. We examined the sensitivity of these genes towards 2-aminopurine (2-AP), a known inhibitor of double-stranded (ds) RNA dependent protein kinase. 2-AP has also been reported to inhibit the induction of IFN-beta 1 in response to dsRNA and the genes c-myc and c-fos in fibroblasts. In both MCF-7 and BT-20 cell lines, 2-AP selectively inhibited the IFN-induced gene responses. 2-AP did not affect levels of the oncogene, HER-2/neu Tamoxifen (TAM), an antiestrogenic drug, which is known to inhibit the activity of protein kinase C at high concentrations, did not affect IFN-mediated gene induction. Our data is consistent with the concept that the 2-AP sensitive kinase is primarily associated with the IFN-induced gene systems and that positive and negative growth regulating stimuli in breast cancer may require the participation of distinct kinases.